IN THE CLAIMS:

Please amend the claims as follows:

1. (amended) A method for constructing a nucleic acid library comprising:

   a) obtaining a population of end-labeled double-stranded cDNA molecules;

   b) dividing said population into a first portion and a second portion;

   c) digesting said first portion with at least one sequence-specific endonuclease wherein said first portion is divided into one pool per endonuclease;

   d) digesting said second portion with at least one (Y) endonuclease having a degenerate recognition sequence and fractionating the digested cDNA into YX^z pools where Y is the number of degenerate endonucleases, X is the the extent of degeneracy and z is the number of bases;

   e) isolating nucleic acid fragments from said endonuclease digestions of said first and second portions using said end-labels;

   f) digesting the fragments of said first portion with said at least one endonuclease of d) sequence and fractionating the digested cDNA into YX^z pools where Y is the number of degenerate endonucleases, X is the the extent of degeneracy and z is the number of bases;

   g) digesting the fragments of said second portion with said at least one endonuclease of c) wherein the second portion pools are divided into one pool per endonuclease;

   h) removing labeled nucleic acid fragments from said first and second portions while retaining unlabeled fragments;

   i) adding a population of adapters to each of the pools, said population containing adapters specific for the endonucleases used, wherein each adapter comprises a first region specific to a particular endonuclease used and a second region containing a primer binding site;

   j) hybridizing and ligating said adapters to said unlabeled fragments;

   k) amplifying the fragments using the adapters; and

2

I) separating the amplified fragments by size.

2. (original) The method of claim 1, wherein said at least one sequence-specific endonuclease comprises at least 4 different sequence specific endonucleases.

3. (original) The method of claim 1, wherein said at least one sequence-specific endonuclease comprises at least 6 different sequence specific endonucleases.

4. (original)The method of claim 1, wherein said at least one sequence-specific endonuclease is selected from the group consisting of at least one endonuclease having a 4 base recognition sequence, at least one endonuclease having a 5 base recognition sequence and at least one endonuclease having a 6 base recognition sequence.

5. (original) The method of claim 3, wherein said at least one sequence-specific endonuclease is selected from the group consisting of *Apa* LI, *Bam* HI, *Eco* RI, *Hind* III, *Nco* I, and *Xho* I.

6. (original) The method of claim 1, wherein said at least one endonuclease having a degenerate recognition sequence produces fragments comprising unpaired overhangs containing N^m unique sequences where N is the extent of degeneracy and is an integer between 2 and 4, and m is the number of bases in said unpaired overhang and is an integer between 2 and 6.

7. (original) The method of claim 6, wherein N^m equals at least 64.

8. (original) The method of claim 7 wherein said endonuclease is *Bsl* I.

9. (original) The method of claim 1, further comprising sequencing the separated fragments of I).

10. (original) The method of claim 1, further comprising quantifying the separated fragments of I).

11. (original) The method of claim 1, wherein said primer binding region of said adapters does not have significant homology to sequences known to be in said population of nucleic acid molecules.

12. (original) The method of claim 11, wherein said primer binding regions of said adapters comprise no more than 10 different sequences.

13. (original) The method of claim 12, wherein said primer binding region comprise no more than two different sequences.

14. (original) The method of claim 1, wherein said end-labeled nucleic acid molecules are obtained by a method comprising, isolating polyA mRNA from a cell; hybridizing a 5' end labeled an oligo dT primer to said polyA m RNA; synthesizing a first cDNA strand by extension of said primer; and synthesizing a second cDNA strand by nick translation to produce double stranded cDNA.

15. (original) The method of claim 14, wherein said oligo dT primer has a sequence comprising L-$(T)_n$VN, where L is a label at the 5' end of said primer and n is an integer between 4 and 50.

16. (original) The method of claim 14, wherein said at least one sequence-specific endonuclease comprises at least 4 different endonucleases.

17. (original)The method of claim 14, wherein said at least one sequence-specific endonuclease is selected from the group consisting of at least one endonuclease having a 4 base recognition sequence, at least one endonuclease

5

4

having a 5 base recognition sequence and at least one endonuclease having a six base recognition sequence.

18. (original) The method of claim 14, wherein said at least one sequence-specific endonuclease comprises at least 6 different endonucleases.

19. (original) The method of claim 18, wherein said at least one sequence-specific endonuclease is selected from the group consisting of *Apa* LI, *Bam* HI, *Eco* RI, *Hind* III, *Nco* I, and *Xho* I.

20. (original) The method of claim 14, wherein said at least one endonuclease having a degenerate recognition sequence produces fragments comprising unpaired overhangs containing N^m unique sequences where N is the extent of degeneracy and is an integer between 2 and 4, and m is the number of

5   bases in said unpaired overhang and is an integer between 2 and 6.

21. (original) The method of claim 20, wherein N^m equals at least 64.

22. (original) The method of claim 21 wherein said endonuclease is *Bsl* I.

10

23. (original) The method of claim 14, wherein said label is biotin.

24. (original) The method of claim 14, wherein isolating and removing of end-labeled nucleic acid molecules is by particles that bind said end-labeled

15   nucleic acid molecules.

25. (original) The method of claim 24, wherein said end-label is biotin and said particles comprise avidin or strepavidin.

20   26. (original) The method of claim 14, further comprising sequencing the separated fragments of I).

5

27. (original) The method of claim 14, further comprising quantifying the separated fragments of I).

28. (amended) A method for constructing a nucleic acid library comprising:

a) obtaining a population of 3' end-labeled double-stranded cDNA molecules by a method comprising, isolating polyA mRNA from a cell; hybridizing
5   a 5' end labeled primer containing an oligo dT tail to said polyA m RNA; synthesizing a first cDNA strand by extension of said primer; and synthesizing a second cDNA strand by nick translation to produce a double stranded cDNA;

b) dividing said labeled population into a first portion and a second portion;

c) digesting said first portion with at least one sequence-specific
10   endonuclease selected from the group consisting of at least one endonuclease having a 4 base recognition sequence, at least one endonuclease having a 5 base recognition sequence and at least one endonuclease having a six base recognition sequence wherein said first portion is divided into one pool per endonuclease;

15   d) digesting said second portion with at least one endonuclease having a degenerate recognition sequence wherein said endonuclease produces fragments comprising unpaired overhangs containing N^m unique sequences where N is an integer between 2 and 4, m is an integer between 2 and 6, and N^m equals at least 64 and fractionating the digested cDNA into YX^z pools where Y is
20   the number of degenerate endonucleases, X is the extent of degeneracy and z is the number of bases;

e) isolating nucleic acid fragments from said endonuclease digestions of said first and second portions using said end-labels;

f) digesting the fragments of said first portion with said at least one
25   endonuclease of d) and fractionating the digested cDNA into YX^z pools where Y is the number of degenerate endonucleases, X is the extent of degeneracy and z is the number of bases ;

6

g) digesting the fragments of said second portion with said at least one endonuclease of c) <u>wherein said first portion is divided into one pool per</u>

30 <u>endonuclease;</u>

h) removing labeled nucleic acid fragments from said first and second portions while retaining unlabeled fragments;

i) adding a population of adapters <u>to each of the pools</u>, said population containing adapters specific for at least some of the endonucleases used,

35 wherein each adapter comprises a first region specific to a particular endonuclease used and a second region containing a primer binding site, said primer binding sites comprising no more than 10 different sequences, said sequences lacking significant homology to sequences known to be in said population of nucleic acid molecules;

40 j) hybridizing and ligating said adapters to said unlabeled fragments;

k) amplifying said unlabeled fragments using the adapters; and

l) separating the amplified fragments on the basis of size.

29. (original) The method of claim 28, wherein said at least one sequence-specific endonuclease comprises at least 4 endonucleases.

30. (original) The method of claim 28, wherein said at least one sequence-specific endonuclease comprises at least 6 endonucleases.

31. (original) The method of claim 30, wherein said at least one sequence-specific endonuclease is selected from the group consisting of *Apa* LI, *Bam* HI, *Eco* RI, *Hind* III, *Nco* I, and *Xho* I.

32. (original) The method of claim 28, wherein said at least one endonuclease having a degenerate recognition sequence is *Bsl* I.

33. (original) The method of claim 28, wherein said at least one sequence-specific endonuclease is selected from the group consisting of *Apa* LI, *Bam* HI, *Eco* RI, *Hind* III, *Nco* I, and *Xho* I, and said at least one endonuclease having a degenerate recognition sequence is *Bsl* I.

34. (original) The method of claim 28, where in said adapters comprise a common primer binding site.

35. (original) The method of claim 28, further comprising sequencing the separated fragments of 1).

36. (original) The method of claim 28, further comprising quantifying the separated fragments of l).

37. (original) The method of claim 28, wherein said label is biotin.

38. (original) The method of claim 28, wherein isolating and removing of end-labeled nucleic acid molecules is by particles that bind said end-labeled nucleic acid molecules.

39. (original) The method of claim 38, wherein said end-label is biotin and said particles comprise avidin or strepavidin.

40-94. (canceled without prejudice)

40

95. (amended) A method for constructing a nucleic acid library comprising:

a) obtaining a population of double stranded cDNA wherein cDNA molecules contained in said population contain a detectable label on their 3' end;

b) digesting said double-stranded cDNA with at least one restriction endonuclease having a degenerate recognition sequence comprising at least one degenerate base, wherein said digestion creates a single-stranded portion or overhang containing a region having the formula N^m, where N is the extent of degeneracy and m is the number of degenerate bases in said single stranded portion or overhang to produce digestion fragments and fractionating the digested cDNA into YX^z pools where Y is the number of degenerate endonucleases, X is the extent of degeneracy and z is the number of bases ;

c) adding a population of adapters to each of the pools, said adapters specific for the at least one endonuclease used;

d) hybridizing and ligating said adapters to the 5' end of said digestions fragments;

e) separating said 3' end digestion fragments using said detectable label;

f) amplifying said 3' end digestion fragments;

g) separating said amplified digestion fragments on the basis of size.

41

40

96. (original) The method of claim 95, wherein said adapters contain first region specific to a particular endonuclease and a second primer binding region common to all adapters.

42

40

97. (original) The method of claim 95 wherein N^m equals at least 16.

43

42

98. (original) The method of claim 97, wherein said at least one endonuclease is _BsaJ_ I.

9